REMARKS

Claims 1-11, 17-30, 33-69 have been canceled without prejudice or disclaimer. Claims 12, 31, 32, 70, and 71 have been amended. Claims 72-89 have been added. Support for these new claims can be found in the specification and in the original claims.

Priority

Applicants take no position on the merits of Examiner's statement, "the provisional application upon which priority is claimed fails to provide adequate written description support under 35 U.S.C. 112 ..." and reserve the right to contest the statement at a later date.

Specification

This amendment includes a substitute specification.

Tables 7 and 8 have been amended so as to replace "?" in the sequence listings with "X."

Applicants used the term "BLyS" to refer to B Lymphocyte Stimulator Protein in the original specification. Applicants have amended the specification to replace all references to "BLyS" with "BLSP," an abbreviation for "B Lymphocyte Stimulator Protein." Thus, Applicants respectfully request the Examiner to withdraw this objection to the specification.

Information Disclosure Statement

As the Examiner requested, Applicants are enclosing copies of references which were previously provided in the Information Disclosure Statement of September 3, 2002.

Election/Restrictions

Applicants take no position on the merits of the final restriction by the Examiner, but reserve the right to contest the Examiner's assertions at a later date.

Note that SEQ ID NO:446 and SEQ ID NO:448 are related to some degree (subscripts have been removed below to illustrate the spacing):

Asp-X-Leu-Thr (SEQ ID NO:446)

X-X-Asp-X-Leu-Thr-X-Leu-X-X (SEQ ID NO:448)

This relationship enables claim 85 to properly depend from 83.

Claim Rejections

The Examiner has rejected all of the pending claims. Applicants will now address the rejections seriatim. The Examiner's remarks are quoted in small bold face type.

Claim Scope

The Examiner commented, on page 8 of the most recent Action, that:

The teachings of the specification are limited to families of BLyS™ binding polypeptides of less than 18 amino acids that bind BLyS™.

The teachings of the specification are not so limited. Moreover, the BLSP binding polypeptide referred to in claim 12 is not limited in size to less than 18 amino acids. Claim 12 indicates that "the BLSP binding polypeptide *comprises* an amino acid sequence selected from the group consisting of ..." (emphasis added). Because the term "comprise" is open-ended, the polypeptide used in the claimed method is not limited by a particular size.

Rejections under 35 U.S.C. § 101

The Examiner asserts that:

Claims 1, ,2, 3, 5, 12, 13, 15, 17, 18, 19, 21-32, 67, 68, 69 and 71 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a *specific and substantial* or a well established utility ...

The specification contemplates that the mere binding of Blys™ provides for treatment of a variety of diseases or disorders, *in vitro* or *in vivo* as recited above.

This is a utility rejection. According to the Utility Examination Guidelines (66 Fed. Reg. 1092-1099 (Jan. 5, 2001); hereinafter "Utility Guidelines"), the Examiner first determines if the claims have a well-established utility (*Id.* at 1098). The Applicants do not concede that the

claimed therapeutic methods lack a well-established utility. Note as a general matter, page 4 of the Revised Interim Utility Guidelines Training Materials (available at http://www.uspto.gov/web/menu/utility.pdf; hereinafter "Training Materials") states:

> IV) Treatment- Since most diseases or conditions can be treated, rejections under 35 U.S.C. § 101 for treatment claims should **rarely be made**. [emphasis added]

The Examiner has not established that the claimed therapeutic methods belong in the exceptional category reserved for therapies of untreatable diseases.

Even so, if there is not a well-established utility, according to the Office's Utility Guidelines, 66 Fed. Reg. at 1098, the Examiner must then:

> 2. Review the claims and the supporting written description to determine if the applicant has asserted for the claimed invention any **specific** and **substantial** utility that is **credible**: (a) If the applicant has asserted that the claimed invention is useful for any particular practical purpose (*i.e.,* it has a "**specific** and **substantial** utility") and the assertion would be considered **credible** by a person of ordinary skill in the art, do not impose a rejection based on lack of utility. [emphasis added]

See also MPEP § 2107. The three prongs of the utility requirement, according to the Office, are (i) "specific" utility, (ii) "substantial" utility, and (iii) "credible" utility. The rejection in the Office Action alleges defects in the "specific" and "substantial" prongs (pages 9-10), but not in "credible" prong (see page 11).

The issues of (i) "specific" and (ii) "substantial" utility are addressed in turn:

(i) Specific Utility

In the context of the utility requirement, "specific" is congruent with "particularized." This is evident from MPEP § 2107.01, which defines "specific utility" as follows:

> A "specific utility" is *specific* to the subject matter claimed. This contrasts with a *general* utility that would be applicable to the broad class of the invention. Office personnel should distinguish between situations **where an applicant has disclosed a specific use** for or application of the invention and situations where the applicant merely indicates that the invention may prove useful without

> identifying with specificity why it is considered useful. For example, indicating that a compound may be useful in treating unspecified disorders, or that the compound has "useful biological" properties, would not be sufficient to define a specific utility for the compound. [emphasis added]

With respect to the method of claim 12, **the applicants have disclosed a specific use** – the treatment of an immune system disorder. An immune system disorder is not an "unspecified disorder," since immune system disorders are a well characterized class of disorders. Further, the specification provides examples of such disorders, e.g., at page 13, beginning at line 10. Thus, an assertion that claim 12 lacks a "specific" utility cannot stand.

This view is further reinforced by the Training Materials. Example 1 of the Training Materials relates to treating a microbe X infection with compound A. The Training Materials state:

> Since microbe X infection is a known infection, and the treatment claimed is directed to a *particular* combination of treatment and agent, the utilities of preventing or treating the infection define specific and particular uses, and are therefore specific utilities. [emphasis in original]

No different from this example, claim 12 is directed to a particular combination of treatment since claim 12 includes treating immune system diseases and disorders (which are known diseases and disorders), with BLSP binding polypeptides with explicit structural properties.

The Examiner contends on page 9 of the Action:

> **The relationship between BLys™, its receptors or activity thereof and the plethora of diseases and disorders is hypothetical and lacks evidentiary support either in the art or in this specification at the time of filing and such lacks specific utility.**

The Examiner is alleging that the "relationship between BLyS™ . . . and diseases" is "hypothetical." But, no facet of "specific" utility requires a relationship between a therapeutic agent, its target, and a disease or some standard of evidentiary support. MPEP § 2107.01 does state that:

> A general statement of diagnostic utility, such as diagnosing an unspecified disease, would ordinarily be insufficient absent a disclosure of what condition can be diagnosed. Contrast the situation where an applicant discloses a specific biological activity and reasonably correlates

> that activity to a disease condition. Assertions falling within this latter category are sufficient to identify a specific utility for the invention.

This text does not require any particular threshold correlation for all method claims. Rather, the text refers to one example of a **diagnostic** that has a correlation to a specified condition to contrast another example where the **diagnostic** returns no information about a specified condition. The point is that, without a specified condition, there is no use for a patient to receive a diagnosis, since a diagnosis of something unspecified would have no informational value. The Office's own directives in the Training Materials that "rejections under 35 U.S.C. § 101 for treatment claims should rarely be made" further compels the understanding that MPEP § 2107.01 has little, if any, relevance for therapeutic methods.

Thus, to reiterate, the requirement for a "specific utility" for a therapeutic method is one for "specified," i.e., "particularized" combinations of agents and disorders. Immune system diseases and disorders are a well studied and characterized class of diseases and disorders. The dependent claims further delineate examples of such diseases and disorders. It cannot be contended that immune system diseases and disorders are not "specified" or "particularized."

The Applicants respectfully submit that the requirement for a "specific utility" is more than adequately met since the claims refer to a particularized combination of agents and disorders.

(ii) Substantial Utility

Next, the method claims have substantial utility. According to MPEP § 2107.01:

> A substantial utility defines a "real world" use ... For example, both a therapeutic method of treating a known or newly discovered disease and an assay method for identifying compounds that themselves have a "substantial utility" define a "real world" context of use.

The claims provide methods of treating immune system diseases and diseases. By its very terms, the MPEP defines therapeutic methods as *per se* possessing "substantial utility." The claims are therapeutic methods and therefore, in accord with MPEP § 2107.01, have a "real world" context of use and thus, "substantial utility."

The Training Materials provide examples of insubstantial utilities that are throw-away uses. None of these examples even remotely approaches the claimed therapeutic methods.

The example, on page 14 of the Training Materials, is an example of a claim with a substantial utility. This method relates to treating a microbe infection with compound A and states, "[t]he characterization of disease as a common infection establishes the presumption that the asserted utilities have a 'real world' context." Since immune system disorders, like infections, are real world problems, the method of the claim 12 has a "real world" context. Thus, the claims have "substantial utility."

The Applicants have carefully reviewed the Office's policies with respect to the utility requirement and have traversed the two grounds that the Office Action relies upon for its utility rejection of the presently amended claims by applying the Office's own policies.[1] Accordingly, the Applicants respectfully submit that the utility rejection should be withdrawn.

35 U.S.C. § 112 Enablement

Claims 1, ,2, 3, 5, 12, 13, 15, 17, 18, 19, 21-32, 67, 68, 69 and 71 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

This enablement reject depends entirely on the utility rejection, addressed above. The Applicants respectfully submit that the enablement rejection can be withdrawn in view of the Applicant's arguments with respect to the 35 U.S.C. § 101 rejection.

[1] Note that the Applicants have assumed *arguendo* that the Office's policies are a correct interpretation of the statute. However, the Applicants reserve the right to contest the validity of these policies at a later date.

35 U.S.C. § 112 Written Description

Claims 1,2, 3, 5, 12, 13, 15, 17, 18, 19, 21-32, 67 and 68 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement.

The claims have been amended. In particular, claim 12 has been amended to recite limitations from claim 69. Since the Examiner determined that the above written description rejection does not applied to claim 69, it likewise would not apply to amended claim 12. Applicants respectfully request that the rejections for lack of written description be withdrawn.

35 U.S.C. § 112 Second Paragraph

Claims 21-24, 29, 31, 67 and 69 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In each of the recited claims, the claims require "contacting an effective amount of BLyS™ binding polypeptide with BLyS. However, in order to inhibit/reduce a B cell activity or increase lifespan, B cells themselves must be present. Therefore, mere contacting of BLyS™ binding polypeptide with BLyS™ does not provide for any activity but binding. Clarification is required.

Claims 21-24, 29, 67, and 69 have been cancelled without prejudice. Without conceding the point, the Applicants have amended claim 31 to depend from claim 12. Since claim 12 refers to administering a BLSP binding polypeptide to an animal, the Examiner's concern that no B cells would be present is obviated.

Rejections under 35 U.S.C. § 102

Again, claim 12 has been amended to include limitations from claim 69. None of the art-based rejections were applied to claim 69. Accordingly, claim 12, as amended, is free of the art applied by the Examiner. Note, however, that the Applicants do not concede that the rejections made under § 102 have merit.

Conclusion

Applicants respectfully submit that all claims are now in condition for allowance which action is expeditiously requested. The Applicant does not concede any positions of the Examiner

that are not expressly addressed above, nor does the Applicant concede that there are not other good reasons for patentability of the presented claims or other claims. All amendments and cancellations are made without prejudice and disclaimer and may be made for reasons not explicitly stated or for reasons in addition to ones stated.

Enclosed is a $1020 check for the Petition for Extension of Time fee. Please apply any other charges or credits to deposit account 06-1050, referencing Attorney Docket No. 10280-080001.

Respectfully submitted,

Date: 14 Jan. 2005

Ramon K. Tabtiang, Reg. No. 55,658

Fish & Richardson P.C.
225 Franklin Street
Boston, MA 02110-2804
Telephone: (617) 542-5070
Facsimile: (617) 542-8906

21004767.doc